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A Proposal for Amino Acid Dependent Main-Chain Torsion-Energy Terms for Protein Force Fields
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A force field is widely used in the field of molecular simulations for biomolecular systems and is determined by an atomic model based on classical mechanics. Many commonly used force fields for protein systems such as AMBER, CHARMM, GROMACS, OPLS, and ECEPP have amino-acid-independent force-field parameters of main-chain torsion-energy terms. Here, we propose a new type of amino-acid-dependent torsion-energy terms in the force fields. As an example, we applied this approach to AMBER ff03 force field and determined new amino-acid-dependent parameters for ψ and ψ' angles for each amino acid by using our optimization method, which is based on the minimization of some score functions by simulations in the force-field parameter space. The score functions were derived for the protein coordinate data in the Protein Data Bank (PDB) [1]. In order to test the validity of the new force-field parameters, we then performed folding simulations of α-helical and β-hairpin peptides, using the optimized force field. The results showed that the new force-field parameters gave structures more consistent with the experimental implications than the original force field.
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Image Charge Solvation Model (ICSM) with Improved Boundary Conditions
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In previous work the Image Charge Solvation Model (ICSM) [1] was introduced as an alternative way to simulate bulk properties of solutions. The ICSM consists of a spherical cavity of explicit solvent embedded in a continuum dielectric medium, and solves the electrostatic interactions accurately and more efficiently than the Particle Mesh Ewald (PME) method on large scales. In spite of the success of the model in simulating a pure water system, and extremely dilute ionic solutions [2], periodic boundary conditions create unphysical charge-charge correlations at finite ion concentrations. Although expanding the system size can reduce these extraneous correlations to negligible levels in principle, the PME method remains more efficient on large scales. In this work we re-evaluate the applied boundary conditions at the cavity wall to correct the problem at its origin, which is related to torques on water molecules due to the electrostatic reaction field [3]. Here, we apply a mean field force representing bulk media outside the cavity, and a self-correcting torque field is introduced to enforce translational symmetry. Our modified ICSM maintains accuracy, performs more efficiently than previously and removes the primary cause of spatial correlations between ions.
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Development of the Charmm Drude Polarizable Force Field for the Study of Ion Interactions in Biological Systems
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Ions play several crucial roles in the structure and function of biological systems: maintaining homeostasis, protein activation and stabilization, and cell electrophysiology and signaling. Molecular dynamics simulations are commonly employed to study ion-protein interactions. Since ions frequently have greater charge densities than the surrounding solvent and protein, they induce a dipole on adjacent molecules and moieties. To some degree, this is implicitly modeled within conventional additive atomic charge force fields. However, polarizable force fields have a considerable advantage over the traditional effective atomic charge force fields in situations where a charge dense species is solvated in a highly polarizable environment, and particularly where a polarizable molecule is solvated by an asymmetric charge density. The presented work describes our effort towards a systematic and more realistic modeling of ions within the framework of the all-atom CHARMM Drude polarizable force field, which is suitable for modeling large biological systems. By calibrating with respect to in vacuo, ab initio gas phase cluster geometries and energetics, as well as the condensed phase thermodynamic properties such as solvation free energy of neutral salts, we have developed polarizable ion parameters that provide specific representation of the many-body polarization effects in biological systems. We have characterized and parametrized the interaction between ions and amino acid side chains (e.g., serine), as well as the highly polarizable protein backbone, which is often found exposed to the interior of transmembrane ion channels. The new force field is used to characterize the binding of barium into the selectivity filter of the KcsA K^+ channel and explore the factors governing the blockade of ion-selective channels by extremely charge-dense multivalent cation

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A Reparametrized Implicit Solvent Model for Accurate Computation of Hydration Free Energies
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While solvation plays an important role in many chemical and biological processes, detailed solvent behavior is typically of much less interest than the effect of the solvent on the solute. Although explicit solvent treatment provides a very accurate description of the considered system, it is not necessary for many applications and can be replaced by implicit solvent models. A typical application is the computation of hydration free energies for small molecules. However a recent study [1] showed that there is still a gap between the accuracy of implicit models typically used in biomolecular simulations and explicit solvent treatment. To address this issue we have reparametrized an implicit solvent model consisting of a generalized Born term to model polar solvation and an extended nonpolar term that models cavity formation and Lennard-Jones interactions with water. When fitted to experimental hydration free energies of a large set of 499 small molecules, the model is able to reproduce hydration free energies with a similar error than those derived from explicit solvent computation, while still offering some degrees of freedom in the fit parameters. To test the transferability of the resulting model, we have applied it to the prediction of hydration free energies of Glycine-X-Glycine tri-peptides. This model will be part of the SIMONA [2] simulation package.
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2598-Pos Board B617
Multi-Level and Interleaved Poisson-Boltzmann (MLIPB) Method for Parallel Computing of the Electrostatics and its Application in Delphi
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Electrostatic potential and energies originating from the charge distribution within biomolecules have great impact on intra- and inter-molecular interactions. Due to the enormous importance of electrostatics in molecular biology, calculating the electrostatic potential and corresponding energies has become a standard computational approach to study biomolecules and nano-objects immersed in water and salt phase or other media. However, the electrostatics of large macromolecules and macromolecular complexes may not be obtainable via explicit methods and even the standard continuum electrostatics methods may not be applicable due to high computational and memory requirements. Here we will present a new multi-level (parallelization is achieved at different levels of the algorithm) and interleaved (parallelization is implemented by interleaving the computational tasks) method, the MLIPB method, to parallelize standard methods for computing electrostatics potential and energies in the framework of Poisson-Boltzmann equation (PBE). The MLIPB method is implemented in the popular software DelPhi, resulting in speedup of several folds without compromising accuracy or imposing additional assumptions. As a demonstration of efficiency and capability of this methodology, electrostatic potential and energies are calculated to illustrate the pathway of electron transfer between the component complexes and cytochrome c binding in the bovine mitochondrial supercomplex. This work is supported by NIH grant R01GM093937.